

*REMARKS/ARGUMENTS**The Pending Claims*

Claims 1-17 and 69-77 are pending currently and are directed to a composition comprising particulate tricalcium phosphate (TCP). Reconsideration of the pending claims is respectfully requested.

*The Amendments to the Claims*

Claims 1 and 71 have been amended to recite that the particulate tricalcium phosphate is chemically-precipitated tricalcium phosphate having an average particle size of about 5  $\mu\text{m}$  or less, an average crystal size of about 250 nm or less and a surface area of about 20  $\text{m}^2/\text{g}$  or greater. This amendment is supported by the specification at, *e.g.*, paragraphs [0009], [0021], [0028], and [0030].

New claims 74-77 have been added. New independent claim 76 has been added and recites a composition comprising calcined particulate tricalcium phosphate (TCP) having an average particle size of about 5  $\mu\text{m}$  or less, an average crystal size of about 250 nm or less and a surface area of about 40  $\text{m}^2/\text{g}$  or greater, wherein the TCP composition can be consolidated to form a TCP article having a compressive strength of about 50 MPa or greater. This amendment is supported by the instant specification at, *e.g.*, paragraph [0026] and Example 7. New claims 74, 75, and 77 depend from claims 1, 71 and 76 respectively, and recite that the particulate tricalcium phosphate is  $\alpha$ -TCP as supported by the instant specification at, *e.g.*, paragraphs [0010] and [0038].

No new matter has been added by way of these amendments.

*Summary of the Office Action*

Claims 1-7, 12-14, 17 and 69-73 stand rejected under 35 U.S.C. § 103(a) as obvious over Kawamura et al. (i.e., U.S. Patent 4,717,556) in view of Tanaka et al. (i.e., U.S. Patent 6,441,073). Claims 8-11 stand rejected under 35 U.S.C. § 103(a) as obvious over Kawamura et al., Tanaka et al., and Kijima et al. (i.e., U.S. Patent 5,185,177). Claims 15 and 16 stand

rejected under 35 U.S.C. § 103(a) as obvious over Kawamura et al., Tanaka et al., and Dalal et al. (i.e., U.S. Patent 6,949,251).

*The Obviousness Rejections*

The obviousness rejections are respectfully traversed.

A. *Kawamura et al.*

Kawamura et al. fails to disclose a *chemically-precipitated* particulate tricalcium phosphate having an average particle size of about 5  $\mu\text{m}$  or less, an average crystal size of about 250 nm or less and a surface area of about 20  $\text{m}^2/\text{g}$  or greater. In addition, Kawamura et al. fails to disclose a *calcined* particulate tricalcium phosphate having an average particle size of about 5  $\mu\text{m}$  or less, an average crystal size of about 250 nm or less and a surface area of about 40  $\text{m}^2/\text{g}$  or greater.

Kawamura et al. is directed to a  $\beta$ -tricalcium phosphate prepared by a mechanochemical process involving preparing a slurry of hydrogen calcium phosphate and calcium carbonate powders in water and subjecting the slurry to attrition. *See* Abstract, col. 2, ll. 31-49; col. 3, ll. 29-43, and Example 1. One of ordinary skill in the art will recognize that “attrition” is a mechanochemical process in which a chemical reaction occurs as a result of the mechanical action of an attrition mill. In this regard, Kawamura et al. teaches that “[i]n consequence of the attrition, the hydrogen calcium phosphate and the calcium carbonate are gradually dissolved in water and the reaction between these components proceeds similar to a homogeneous reaction, giving rise to microfine  $\beta$ -tricalcium phosphate hydrate particles of homogeneous composition.” *See* col. 3, ll. 34-40. According to Kawamura et al., the chemical reaction proceeds only as a consequence of the mechanical action of the attrition process, i.e., the attrition causes the solubility which allows the chemical reaction.

Kawamura et al. contrasts the mechanochemical process of attrition described therein to a conventional wet chemical approach involving a neutralizing reaction between calcium hydroxide and phosphoric acid, and a reaction of calcium nitrate solution with aqueous hydrogen ammonium phosphate solution. Kawamura et al. describes such methods as “conventional” and as suffering numerous “disadvantages” including low purity and poor crystal formation. *See* col. 1, ll. 46, to col. 2, ll. 12. Thus Kawamura et al. teaches away

from chemically-precipitated particulate tricalcium phosphate as recited in the pending claims. Indeed one of ordinary skill in the art, following the teaching of Kawamura et al., would be unable to prepare a chemically precipitated tricalcium phosphate particulate composition having the crystal size and surface area described by Kawamura et al.

The instant specification describes particulate tricalcium phosphate prepared using such a wet chemical approach in which a calcium salt (*e.g.*, calcium hydroxide or calcium nitrate) and a phosphate source (*e.g.*, phosphoric acid or hydrogen ammonium phosphate), but which has a an average particle size of about 5  $\mu\text{m}$  or less, an average crystal size of about 250 nm or less and a surface area of about 20  $\text{m}^2/\text{g}$  or greater. Nothing in Kawamura et al. teaches a *chemically-precipitated* particulate TCP having these properties.

Moreover, nothing in Kawamura et al. teaches or suggests a calcined particulate tricalcium phosphate (regardless of preparation method) having an average particle size of about 5  $\mu\text{m}$  or less, an average crystal size of about 250 nm or less and a surface area of about 40  $\text{m}^2/\text{g}$  or greater as recited in newly added claim 76. Rather Kawamura et al. teaches calcined TCP having surface areas of only 24  $\text{m}^2/\text{g}$ , 26.8  $\text{m}^2/\text{g}$ , 27.4  $\text{m}^2/\text{g}$ , or 30  $\text{m}^2/\text{g}$ . *See, e.g.*, col. 3, ll. 16-20; col. 4, ll. 13-17; ll. 56-58; col. 5, ll. 12-14. There is nothing in Kawamura et al. that teaches the production of particulate tricalcium phosphate, which following calcination, has a surface area of about 40  $\text{m}^2/\text{g}$  or greater.

In addition, nothing in Kawamura et al. teaches a composition comprising  $\alpha$ -TCP. Indeed, the title of the invention of Kawamura et al. is "Method For Producing Of  $\beta$ -Tricalcium Phosphate." *See Title*. Dependent claims 74, 75 and 77 are directed specifically to particulate  $\alpha$ -TCP. One of ordinary skill in the art given the teaching of Kawamura et al. would be unable to prepare  $\alpha$ -TCP having the claimed crystal size, particle size, and surface area.

B. *Tanaka et al., Dalal et al., and Kijima et al.*

Tanaka et al., Dalal et al., and Kijima et al. each fail to cure the deficiencies of Kawamura et al.

As discussed in the Reply to Office Action dated November 27, 2007, Tanaka et al. is directed to a biomaterial comprising particulate calcium phosphate, such as a tricalcium phosphate, which is compounded with a copolymer of lactic acid, glycolic acid, and caprolactone that provides the particulate calcium phosphate with strength and rigidity. *See, e.g.,* col. 2, ll. 23-25. Tanaka et al. is silent with respect to the crystal size and surface area of the calcium phosphate material that is to be combined with the copolymer, although one of ordinary skill in the art will appreciate that in order to achieve such high solids loadings, the tricalcium phosphate surface area would have to be relatively low, on the order of  $\sim 1 \text{ m}^2/\text{g}$ .

Dalal et al. is directed to a  $\beta$ -TCP composition and the use thereof to prepare porous  $\beta$ -TCP granules which can be combined with a binder to form a moldable putty composition. Nothing in Dalal et al. teaches or suggests a TCP composition having the crystal size, particle size, or surface area recited by the pending claims.

Kijima et al. is directed to a sintered body of zirconia having a porous, sintered coating comprising a mixture of zirconia and tricalcium phosphate. Nothing in Kijima et al. teaches or suggests a TCP composition having the crystal size, particle size, or surface area recited by the pending claims.

Thus, even if one of ordinary skill in the art were motivated to combine the teachings of Kawamura et al. with Tanaka et al., Dalal et al., and/or Kijima et al., which they would not be, such combination would not provide a chemically-precipitated and/or calcined particulate TCP composition having the particle size, crystal size, and surface area recited in the pending claims. Because the combination of Kawamura et al. with Tanaka et al., Dalal et al. and/or Kijima al. fails to teach or suggest each and every element of the invention recited in the pending claims, the obviousness rejections are improper and should be withdrawn.

### *Conclusion*

Applicants respectfully submit that the patent application is in condition for allowance. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,

A handwritten signature in cursive script, reading "Caryn C Borg-Breen", written in black ink.

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